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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/943,780 | 08/30/2001 | Kevin P. Baker | P2548P1C10 | 2570 |

28442 7590 01/27/2005

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| EXAMINER | |
|---|---|
| HELMS, LARRY RONALD | |
| **ART UNIT** | **PAPER NUMBER** |
| 1642 | |

DATE MAILED: 01/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/943,780 | BAKER ET AL. | |
| | Examiner | Art Unit | |
| | Larry R. Helms | 1642 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *08 November 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *25-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

1. Claims 25, 26, 35-36 have been amended.

2. Claims 25-36 are pending and under examination.

3. The text of those sections of Title 35 U.S.C. code not included in this office action can be found in a prior Office Action.

***Response to Arguments***

4. The rejection of claims 25-36 under 35 U.S.C. 101 because the claimed invention is not supported by either a substantial asserted utility or a well established utility is maintained.

The response filed 11/8/04 has been carefully considured but is deemed not to be persuasive. It is noted that applicants previously argued that the claimed polypeptides would be useful in creating degenerate oligonucleotide probes for isolation of genomic and cDNA sequences that are amplified in tumors and this argument is not further presented in this response. The response states that the examiner has set the standard for satisfying the utility requirement too high and applicants have previously argued that the polypeptides encoded by the DNAs tested have utility as diagnostic markers for determining the presence of tumor cells in lung and/or colon tumors (see pages 2 to 4 of response). In response to this argument, the only nucleic acid that is overexpressed in tumor is SEQ ID NO:68 and there is no indication that SEQ ID NO:69 or any other polypeptide is overexpressed in tumors.

The response further states that it is general scientific principle that DNA is transcribed into RNA which is translated into protein and cites several references for the assumption (see pages 5-8 of response). In response to this argument, Pollack only teach mRNA amplification, not protein levels, Orntoft et al while showing some correlation of mRNA to protein in a small amount of samples in one cancer, showed that protein degradation may be important and this is important for proteins with short half-lives and in liver cells there was a poor correlation between mRNA and protein (see page 44). The comments in Orntoft are important because it is not known what the half-life if any of the claimed polypeptides are and as such whether the claimed polypeptides could be used for diagnostic markers in tumors. Hymen et al only show mRNA overexpression, Varis again only showed mRNA overexpression and this is for genes already known to be amplified (which is also seen in several of the cited references presented such as HER-2neu), Bermont also only show p185 as the overexpressed protein which was also known and demonstrated in several of the cited references in the response, Hu et al also only showed one protein overexpressed of 18 identified. While the references may show some proteins are overexpressed (and some references show the same proteins) and correlate with mRNA levels, the prior art cited by the examiner also showed the unpredictability in the art as far as protein expression correlated with mRNA levels and it appears from the prior art that each gene expression analysis must be performed in order to determine definitively whether protein correlates with mRNA levels. In addition, it appears that the half-life of the protein is important for

use as a diagnostic marker and if a short half-life this would add to the unpredictability of using SEQ ID NO:69 as a diagnostic marker.

The response further states that Pennica et al does not outweigh the teachings of the specification and the references cited by applicants and Pennica supports a utility for the present invention because Pennica et al teaches that gene amplification of WISP-1 strongly correlates with RNA overexpression (see page 9 of response). In response to this argument, again Pennica demonstrates that each gene amplification and correlation to protein overexpression needs to be determined by a case by case basis because even Pennica's three gene expression do not correlate. Specifically the response states that WISP-3 was not amplified and significantly overexpressed (see page 9). However, this was based on gene amplification not protein analysis. While there may be some question as to the data for the WISP-2, this supports the conclusion that each gene must be analyzed individually and a definitive result confirmed for protein expression. Therefore, the art of Pennica et al does support the art that mRNA levels need to be confirmed for protein expression for each gene analyzed.

The response further states that the claimed invention is supported by a substantial utility and summarizes the utility guidelines (see pages 9-11 of response). In response to this argument, the examiner is applying the criteria for utility.

5. The rejection of claims 25-36 rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted

utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention is maintained.

The response filed 11/8/04 has been carefully considured and is deemed not to be persuasive. The response states that the claimed polypeptides have utility as stated above (see page 11-12 of response). In response to this argument, the remarks above address the rejection of 101 and as such one would not know how to use the claimed invention.

6. The rejection of claims 25-26, 33-34 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is maintained.

The response filed 11/8/04 has been carefully considured but is deemed not to be persuasive. The response states that applicants disagree with the examiner that the statement "might be isolated" is a proper ground for rejection and cites MPEP 2163.02 for demonstrating "possession" and applicants have satisfied the written description requirement by first disclosing the structure of SEQ ID NO:68 and 69 and disclose a method for making substitutions and obtaining at least 95% sequence identity to SEQ ID NO:69 and the gene is described by being encoded by a nucleic acid that is amplified in lung or colon tumor (see pages 15). In response to this argument, while SEQ ID NO:68 and 69 are disclosed, they are the only sequences disclosed. While the

specification discloses substitutions there is no examples of such molecules and there is no examples of any nucleic acid except SEQ ID NO:68 which is amplified in tumor.

The response further states that the examiner did not address the arguments of example 13 of the written description guidelines and state that a variant is not adequately described if the claim do not indicate what distinguishing features are shared by the genus, the specification and claim do not place any limit on the number of amino acid substitutions, the claim fail to disclose structural features of the genus, Further the response states that claims 25 and 26 are adequately described because the claims require the polypeptide to be encoded by a nucleic acid that is amplified in tumor and the claims are limited by requiring 95-99% identical to SEQ ID NO:69 and the specification discloses structural features of the genus (see pages 15-16 of response). In response to this argument, the claimed function is that the nucleic acid be amplified in tumor, but this function is attributed to the nucleic acid not the claimed polypeptide, therefore example 13 is not analogous.

The response then argues example 14 again and as such the response to this is the same as the reasons of record. The response then argues that the specification teaches how to find a polypeptide that is 95-99 identical to SEQ ID NO:69 which is encoded by a nucleic acid that is amplified in tumor (see pages 16-17 of response). In response to this argument, the rejection is based on written description and possession and as such it is not based on enablement of how to make or use. Therefore, methods to isolate such does not give one possession. The specification does not provide written description for the claimed polypeptides.

7. The rejection of claims 25-36 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is maintained.

The response filed 11/8/04 has been carefully considured but is deemed not to be persuasive. The response states that PRO357 possesses significant homology to the acid labile subunit of insulin-growth factor and one would know to compare the claimed sequence with the acid labile subunit to minimize amino acid changes even though the acid labile unit is not amplified in tumor it is still a protein and applicants have disclosed conservative substitutions that might be used in modifying the sequence (see pages 18-19 of the response). The response further states that none of the references provided by the examiner contradicts the guidance provided in the specification and Burgess is directed to non-conservative modifications and Lazar teach modifications in conserved regions and Schwartz et al is a non-conservative alteration and Lin does not teach removing the histidine renders the protein non-functional (see page 20 of response). In response to this argument, while the art cited by the examiner does demonstrate the unpredictability in the art of protein chemistry as far as substitutions are concerned, this is underscored by the fact that although the specification compares the PRO357 sequence to the acid labile subunit of insulin-growth factor, there is no evidence that SEQ ID NO:69 has any function at all with the acid labile subunit of insulin-growth factor. Thus one skill in the art would not know

which regions of SEQ ID NO:69 would be conserved or which regions to alter. In addition the specification does not state that SEQ ID NO:69 has any of the functions of the acid labile subunit of insulin-growth factor. Thus, it is unpredictable which if any residues to alter and still retain any activity which is not stated in the specification except that the polypeptide is encoded by a nucleic acid that is overexpressed in lung or colon tumor.

The response further states that the art cited by the examiner for unpredictability in the art for expression of mRNA does not necessarily correlates not predicts polypeptide expression does not contradict or outweigh the evidence discussed above in the 101 rejection (see pages 20-23 of response). In response to this argument, as stated above while the references my show some proteins are overexpressed and correlate with mRNA levels, the prior art cited by the examiner also showed the unpredictability in the art as far as protein expression correlated with mRNA levels and it appears from the prior art that each gene expression analysis must be performed in order to determine definitively whether protein correlates with mRNA levels.

In view of the lack of guidance, lack of examples, and lack of predictability in the art as evidenced from the above references, one skilled in the art would be forced into undue experimentation in order to practice the broadly claimed invention.

***Conclusion***

8. No claim is allowed.

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (571) 272-0832. The examiner can normally be reached on Monday through Friday from 6:30 am to 4:00 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached on (571) 272-0787.

11. Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center telephone number is (703) 308-4242.

Respectfully,

Larry R. Helms Ph.D.

571-272-0832